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ART UNIT	PAPER NUMBER
1652	[REDACTED]

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No. 09/471459	Applicant(s) Fidock, D. Mark
Examiner T. Sadha	Group Art Unit 1652
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—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE —3— MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

- Responsive to communication(s) filed on 9/6/02 (Election)
- This action is FINAL.
- Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- Claim(s) 1-6, 8-12, 16-17, 26-36 is/are pending in the application.
- Of the above claim(s) 3-6, 8-12, 16-28 & 32-35 is/are withdrawn from consideration.
- Claim(s) _____ is/are allowed.
- Claim(s) 1-2, 17, 29-31 & 36 (Sp. SEQ 1DND:5) is/are rejected.
- Claim(s) _____ is/are objected to.
- Claim(s) _____ are subject to restriction or election requirement.

Application Papers

- See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- The proposed drawing correction, filed on _____ is approved disapproved.
- The drawing(s) filed on _____ is/are objected to by the Examiner.
- The specification is objected to by the Examiner.
- The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

- Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- All Some* None of the CERTIFIED copies of the priority documents have been received.
- received in Application No. (Series Code/Serial Number) _____.
- received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

Attachment(s)

- Information Disclosure Statement(s), PTO-1449, Paper No(s). _____ Interview Summary, PTO-413
- Notice of Reference(s) Cited, PTO-892 Notice of Informal Patent Application, PTO-152
- Notice of Draftsperson's Patent Drawing Review, PTO-948 Other _____

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DETAILED ACTION

1. The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1652.
2. The Preliminary Amendment filed December 22,1999 (Paper No. 3) is acknowledged. Applicants' substitute specification identifying the sequences by SEQ ID Nos. has been entered.
- 3.

Election

Applicant's election with traverse of Group I (claims 1-2, 17, 29-31 & 36), species SEQ ID NO : 5 in Paper No. 17 is acknowledged. The traversal is on the ground(s) that Group I & II claims should be combined for examination, since (1) the amino acid sequence(s) of Group I and the nucleotide sequences of Group II are entirely reflective of one another, (2) all the amino acid sequences of Group I are PDE XIV proteins, and all of the nucleotide sequences of Group II encode PDE XIV proteins. As such, any search relevant to one would also perform the task of searching for the other. [In fact, in order to properly and fully search the amino acid sequences of Group I, it will be necessary for the Examiner to search the nucleotide sequences of Group II -]

This is not found persuasive because depending upon the restricted group (I or II) being examined, additional classes/subclasses have to be searched. For example, Group II claims, drawn to nucleic acid encoding a phosphodiesterase, vector , host cell and a method of making the protein, will involve searching for additional class 536 & subclass 23.2 for DNA encoding the enzyme; host cell (class 435, subclass 252.3) & vector (class 435, subclass 320.1) as compared to Group I claims,

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drawn to a phosphodiesterase, will involve searching for only class 435 & subclass 196. This additional searching as explained above would therefore involve undue burden to the Examiner.

Applicants argue that the amino acid sequence(s) of Group I and the nucleotide sequences of Group II are entirely reflective of one another and all the amino acid sequences of Group I are PDE XIV proteins, and all of the nucleotide sequences of Group II encode PDE XIV proteins.

In response it is stated that although the DNA and the protein are related, since the DNA encodes the specifically claimed protein, they are distinct inventions because the protein product can be made by other and materially distinct processes, such as purification from the natural source. Further each of the proteins and the encoding nucleic acid are structurally distinct (requiring a separate sequence search for each of the sequences) and even if encoding an isozymic PDE, have a different level of enzymatic activity.

The requirement is still deemed proper and is therefore made FINAL.

4. Claims 3-6, 8-12, 16, 26-28 & 32-35 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention, the requirement having been traversed in Paper No. 17.

5. ***Priority***

Acknowledgment is made of applicants' claim for priority based on an application filed in United Kingdom on 12.23.98 & 9.17.99.

6. ***Drawings***

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The Draftsman's objection(s) to the drawings is enclosed here in the notice on form PTO-948.

Correction is required.

7. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.
8. Group I (claims 1-2, 17, 29-31 & 36) pertaining to elected species of SEQ ID NO : 5 are under consideration in this examination.
9. ***Claim Rejections - 35 U.S.C. § 112*** (first paragraph)

Deposit Requirement

Claim 17 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that the [plasmid/microorganism/vector] is required to practice the claimed invention. As such the [plasmid/microorganism/vector] must be readily available or obtainable by a repeatable method set forth in the specification, or otherwise readily available to the public. If it is not so obtainable or available, the requirements of 35 U.S.C. 112, first paragraph, may be satisfied by a deposit of the [plasmid/microorganism/vector]. The specification lacks complete deposit information for the deposit of [plasmid/microorganism/vector]. If a deposit was made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicants, or a statement by an attorney of record over his or her signature and registration number, stating that the instant invention will be

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irrevocably and without restriction released to the public upon the issuance of a patent, would satisfy the deposit requirement made herein. If a deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.809 and MPEP 2402-2411.05, Applicant may provide assurance of compliance by affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number showing that (a) during pendency of the application, access to the invention will be afforded to the Commissioner upon request, (b) all restrictions upon availability to the public will be irrevocable removed upon granting of the patent, (c) the deposit will be maintained in a public depository for a period of 30 years, or 5 years after the last request or for the enforceable life of the patent, whichever is longer, (d) a test of the viability of the biological material at the time of deposit (see 37 CFR 1.807) and (e) the deposit will be replaced if it should ever become inviable.

Claim 17 is rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

While deposits of NCIMB Numbers 40995, 40996 & 41027 have been made in accordance Budapest Treaty at a recognized depository; however, an affidavit or declaration [under 37 CFR 1.808] stating that : all restrictions upon availability to the public will be irrevocable removed upon granting of the patent, the deposit will be maintained in a public depository for a period of 30 years, or 5 years after the last request or for the enforceable life of the patent, whichever is longer, and the deposit will be replaced if it should ever become inviable.

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10.

Enablement

Claims 1-2 & 29-31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated PDE of SEQ ID NO: 5 and using cAMP are the substrate, does not reasonably provide enablement for any amino acid sequence of Formula I or a variant, fragment or derivative thereof (claim 1) or isolated PDE_XIV protein that share 75%, 85% or 95% sequence homology to SEQ ID NO : 5. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims. [For convenience, the PDE of the present invention is referred to as PDE_XIV, see specification - page 6].

Claim 1-2 encompass any protein, which by definition of Formula I comprise one or more peptide sequences or amino acids Z1-Z26 (see page 5, substitute specification) or a variant, fragment or derivative thereof; claims 29-31 encompass modifications of SEQ ID NO : 5 by 25%, 15% or 5%. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of proteins fragments or amino acid or phosphodiesterases broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which

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the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of PDE_XIV.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any protein of the formula I or an isolated PDE_XIV with 75, 85 or 90% identity to the enzyme of SEQ ID Nos: 5 because the specification does not establish: (A) regions of the protein structure which may be modified without effecting PDE_XIV activity; (B) the general tolerance of PDE_XIV to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any PDE_XIV residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Further, the phosphodiesterases/isozymes from different sources having varying substrate specificities for cAMP or cGMP and the PDE activity in some tissues could be activated by calcium or calmodulin [Beavo et al. (1995), Physiological Reviews 75(4) : 725-748; also see instant specification, page 1-2]. Therefore, random modifications of the SEQ ID NO : 5 or the fragments or

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derivatives of Formula I, without adequate guidance, may result in a protein with no or entirely diverse PDE activity with different substrate specificity and cofactor requirement.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including PDE_XIV with an enormous number of amino acid modifications of the PDE_XIV of SEQ ID Nos: 5 and retain PDE_XIV activity in the hydrolysis of cAMP as the only substrate for catalysis. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of PDE_XIV having the desired enzymatic characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

11. ***35 U.S.C. § 112, first paragraph (Written Description)***

Claims 1-2 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Claims 1-2 recite [or mean as per definition of formula I] ‘variant, homologue, fragment or derivative of Formula I’. However, no variant, homologue or derivative of Formula I...is given in the specification.

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The specification, however, only provides a single representative species in the generic formula I comprising fragments Z1-Z26. There is no disclosure of any particular structure to function/activity relationship in the single disclosed species to other species where such sequences are conserved in order to establish a relationship among species or modify the sequence(s) of formula I (SEQ ID Nos : 9-22 and the shorter fragments of less than 4 amino acid long, page 5 of the specification) by substitution, deletion or addition (see specification, page 38) or make a polypeptide of an unknown activity. The specification also fails to describe additional representative species of such peptides by any activity other than the identifying structural characteristics recited in Formula I, for which no predictability of activity is apparent. Given this lack of additional representative species, such as the modifications in order to crate a variant, homologue, fragment or derivative of Formula I of and still have some activity and/or utility, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Therefore, the written description requirement is not satisfied.

12. Claim 36 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

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Claim 36, depends upon a non-elected claim 35. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

13. ***Claim Rejections - 35 U.S.C. § 112*** (second paragraph)

Claims 1-2 & 17 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-2 refer to 'Formula I' - where the formula is represented by **any one** of the amino acids or SEQ ID Nos. (Z1-Z26) as disclosed on page 5 of the substitute specification. While such a formula is meaningless, as nothing is calculated or derived from it, it is also indefinite and unclear with respect to Z2, Z3, Z4, Z8, Z19-Z29, which amino acids/peptide sequences have no reference SEQ ID NO : Clarification and assigning of reference SEQ ID NO : will overcome this rejection.

Since Applicants have elected Group I and species SEQ ID NO : 5 for prosecution, it is unclear from the specification which of the DNA sequences encoding SEQ ID NO : 5 is contained in the 3 deposit numbers (NCIMB) of claim 17.

Clarifying the single deposit and limiting the claim to the specific deposit will overcome this rejection.

14. **35 U.S.C. § 101**

35 U.S.C. § 101 reads as follows:

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"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title".

Claims 1-2 & 17 are rejected under 35 U.S.C. § 101 because the claimed invention is directed toward non-statutory subject matter.

In the absence of the hand of man, naturally occurring proteins and/or nucleic acids are considered non-statutory subject matter. *Diamond v. Chakrabarty*, 206 USPQ 193 (1980). This rejection may be overcome by amending the claims 1-2 & 17 to recite wording such as "An isolated amino acid sequence or isolated PDE_XIV".

15. **Priority:** In evaluating the prior art, Applicants were deemed to be entitled to an effective filing date of **9.17.99**, the filing date of foreign application filed in United Kingdom 9922123.6, with respect to the complete or claimed human sequence of PDE_XIV (450 amino acids).

The human sequence of PDE_XIV (SEQ ID NO : 2) as disclosed in United Kingdom 9828603.2, filed 12.23.98, had only **288 amino acids** as compared to instantly claimed human sequence of PDE_XIV (SEQ ID NO : 5) having 450 amino acids. Therefore, United Kingdom 9828603.2, does not qualify for the earlier priority of 12.23.98, because this priority document was lacking an enabling disclosure with respect to the claimed invention. The instant application is therefore not entitled to an effective filing date earlier than **9.17.99**.

Claim Rejections - 35 U.S.C. § 102

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16. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

- (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
- (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2 are rejected under 35 U.S.C. 102(b) as being anticipated by purified amino acids kits (SIGMA; product no. DAA-20, DLAA & LAA-21, for example) comprising individual amino acids. The claims are written so broadly as to be anticipated by the reference.

17. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

- (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

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Claims 1-2, 29-30 & 36 are rejected under 35 U.S.C. 102(e) as being anticipated by Robision et al. (U.S.P. 6,146,876, filing date June 11, 1999). Robision et al. teach a human cyclic nucleotide sequence phosphodiesterase amino acid sequence of (SEQ ID NO : 1) which is 93.8% similar to the claimed amino acid sequence of SEQ ID NO : 5, and therefore having 75% or 85% homology (claims 29-30), or an amino acid sequence that comprises Z17 or SEQ ID NO : 21 (for example) [see sequence alignment of SEQ ID NO : 5 with SEQ ID NO : 1 from U.S.P. 6,146,876, enclosed here], the limitations of claim 1 & 2. Similarly, several amino acids or peptide sequences of Formula I are also comprised by the SEQ ID NO : 1 from U.S.P. 6,146,876. U.S.P. 6,146,876 also teaches a nucleic acid sequence of SEQ ID NO : 2, which is 94.1% similar to Applicants' SEQ ID NO : 6 [which encodes Applicants' human PDE of SEQ ID NO : 5], will therefore hybridize under high stringency conditions to a nucleic acid encoding a PDE protein of claim 36.

The reference anticipates the claims, since all the claim(s) limitations are taught in U.S.P. 6,146,876.

18. No claim is allowed.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tekchand Saidha (Ph.D.) whose telephone number is (703) 305-6595. The examiner can normally be reached on Monday-Friday from 8:15 am to 4:45 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy, can be reached at (703) 308-3804. The fax phone number for this Group in the Technology Center is (703) 308-0294.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.


Tekchand Saidha
Primary Examiner, Art Unit 1652
October 29, 2002